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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/173,864	10/16/98	IVARIE R	24011-0002

HM12/0526
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EXAMINER	
KAUSHAL,S	
ART UNIT	**PAPER NUMBER**
1633	7

DATE MAILED: 05/26/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/173,864	Applicant(s) Ivarie et al
	Examiner Sumesh Kaushal	Group Art Unit 1633

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *19, 21, 25, 27, 29, 33-35, and 41-54* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *19, 21, 25, 27, 29, 33-35, and 41-54* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The instant application claims priority to a Provisional Application No. 60/062172 filed 10/16/97. The preliminary amendment filed on 05/10/99 has been entered. Claims 1-18, 20, 22-24, 26, 28, 30-32 and 36-40 has been canceled and newly filed claims 42-54 has been entered. Claims 19, 21, 25, 27, 29, 33-35, 41 and 42-54 are considered for examination in this office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 50 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim is drawn to a method of post-translational modification of a protein using a vector encoding two sequences. The second coding sequence is capable of providing post translational modification of the protein encoded by the first coding sequence, wherein an internal ribosome entry site element (IRES) is positioned between first and second coding sequence. The method of providing post-translational modification of the proteins deposited in an avian egg is not enabled because specification fails to provide guidance to the claimed method of post-translational modification of any and all proteins deposited into an egg. The specification fails to teach the claimed genetic construct encoding a protein, an IRES element and a second encoding sequence required for post-

translational modification. The specification only exemplified the first coding sequence may encode collagen which would be hydroxylated and made active by an enzyme encoded by the second coding sequence but fail to show such post-translational modification of any protein deposited in an egg (see page 23 lin 23, App. Spec). The state of the art at the time of filing was such that various factor affects the extent of the post translational modification of proteins. For example, besides the type of enzyme used for the post translational modification of collagen, one of the critical factor that regulates the collagen post-translational modification is the ratio of enzyme to substrate in the cell. (Myllya et al, Biochem . J. 196:683-692, 1981, see page 691, col.2 lin.1). The specification fails to provide guidance to a specific modulating enzyme for post translational modification of collagen or any other protein of interest and fails to show the claimed post translational modification of a protein. Furthermore, the specification fails to show the deposition of an exogenous protein in an avian egg, which is post translationally modified using the claimed di-cistronic vector, encoding a protein and a modifying enzyme. Thus, considering the state of the art at the time of filing and the guidance provided in the specification, the skilled artisan at the time of filing would be lacking a reasonable expectation of success, to make an avian egg containing the post translational modified exogenous protein, without an undue amount of experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 50 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims recite a second coding sequence capable of providing post translational modification of a protein encoded by first coding sequence. The claim fails to recite the protein

encoded by first coding sequence and the enzyme required for its post translational modification encoded by the second coding sequence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 27 and 33 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Thoraval et al (Trans. Res. 4:369-376, 1995). Thoraval et al teaches germline transmission of exogenous genes in chickens using helper-free ecotropic avian leukosis virus based vector (see page 371, col.2, table-1 and par.1). Thus, Thoraval et al clearly anticipated the method wherein the introduction of the vector into blastodermal cell is mediated by a retrovirus.

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 19, 21, 25, 27, 29, 34, 35, 41, 42, 44, 47 and 51-54 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Macarthur WC (WO 97/47739, filed 12/18/97). Macarthur teaches a transgenic hen wherein the transgene is expressed in the hen's oviduct and the transgene product is secreted in the egg. The prior art teaches the use of retroviral vectors to where the control element is operatively-linked to transgene and capable of directing the synthesis of a the transgene product in chicken egg white or avian egg yolk using a signal sequence (see page 3, lin.25-

35; page 6, lin.19; page 10, lin.9; page 16, lin.5-25). The cited art also teaches the a transgenic hen wherein the transgene is expressed in the hen's oviduct and the transgene product is secreted in the hen's eggs and/or those of offsprings (page 5, lin.16, page 9, lin.31, page 20, lin.19). The prior art also teaches the transgene products or proteins secreted in the egg where in the encoded genes includes the gene encoding blood proteins, hematopoietic growth factors and lymphopoietic growth factors (page 5, lin 32, page 6, lin.1-7, page 12, lin.27). The cited art also teaches the expression of transgene in the oviduct of a transgenic bird (page 5, lin 15). The prior art also teaches a vector comprising a signal peptide operably linked to a coding sequence (page 12, lin 9, fig-2). The cited art also teaches the injection of a vector or transfected cells producing virus containing a transgene into newly laid chicken eggs and developing oocyte in vivo (page 7, lin 10; page 8, lin.1, page 20, lin.7-11). Thus, Macarthur WC clearly anticipated the invention of instant claims

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 43, 45, 46, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thoraval et al (Trans. Res. 4:369-376, 1995) in view of Kotani et al (Hum. Gene Ther. 5:19-28, 1994). Thoraval et al teaches the germline transmission of exogenous genes in chickens using helper-free ecotropic avian leukosis virus based vector (see page 371, col.2, table-1 and par.1), but does not teach the regulation of transgene expression of by the CMV promotor in ALV vector. Kotani et al

teaches the use of CMV promotor in the retroviral vectors. Thus, Thoraval et al teaching the ALV vector and Kotani et al teaching the use of CMV promotor to regulate the expression of a gene, it would have been obvious to one with ordinary skill in the art to use CMV promotor to regulate the expression of a gene. One would have been also motivated to had CMV promotor in ALV vector because CMV promotor is know to provide a stronger constitutive expression.

Conclusion

Claims 50 are free of the prior art. The art at the time of filing did not teach or suggest the method of post-translational modification of a protein deposited in an egg using a vector encoding two sequences where, the second coding sequence is capable of providing post translational modification of the protein encoded by the first coding sequence, wherein an internal ribosome entry site element (IRES) is positioned between first and second coding sequence.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM . If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brian Stanton Ph.D. can be reached on (703) 308-2801. The fax phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

Sumesh Kaushal
Art Group 1633

BRIAN R. STANTON, PH.D
PRIMARY EXAMINER